IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of :

Ulf TILSTAM, et al. : **Group Art Unit: 1623**

Serial No.: 09/471,040 : **Examiner: Howard V. Owens**

Filed: December 23, 1999 :

For: PROCESS FOR THE PRODUCTION OF FLUDARABINE-PHOSPHATE LITHIUM, SODIUM, POTASSIUM, CALCIUM AND MAGNESIUM SALTS AND PURIFICATON PROCESS FOR THE PROCUTION OF FLUDARABINE-PHOSPHATE AND FLUDARABINE-PHOSPHATE WITH A PURITY OF AT LEAST 99.5%

BRIEF ON APPEAL

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as First Class Mail in an envelope addressed to: Commissioner of Patents, P O Box 1450, Alexandria, VA 22313-1450 on: September 5, 2003
Name: James J. Elbert, Reg. No. 37,702
Signature: [signature]

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Further to the Notice of Appeal filed May 2, 2003, herewith are three copies of Appellants' Brief on Appeal. The attached check includes the statutory fee of $320.00 for the filing of this Brief.

This is an appeal from the decision of the Examiner finally rejecting claims 5-16; see the Final Office Action mailed January 2, 2003. This Brief and a finalized declaration faxed August 28, 2003, constitute a reply to the final rejection. The Brief also provides a summary of multiple teleconferences in July and August 2003.

(1) REAL PARTY IN INTEREST

The above-identified application is assigned of record to Schering Aktiengesellschaft, by virtue of an Assignment recorded February 17, 1999 (Reel 9765/Frame 0834), and who is the real party in interest herein.

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(2) RELATED APPEALS AND INTERFERENCES

Appellants, their legal representative and the assignee are not aware of any related appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the instant appeal.

(3) STATUS OF THE CLAIMS

Claims rejected:	**5-16.**
Claims allowed:	**None.**
Claims canceled:	**1-4.**
Claims withdrawn:	**None.**
Claims on Appeal:	**5-16.**

(4) STATUS OF AMENDMENTS AFTER FINAL

No amendments were filed after final rejection, although a declaration was faxed August 28, 2003.

(5) SUMMARY OF THE INVENTION

Appellants' invention relates to fludarabine phosphate with a purity of at least 99.5%. Prior to Appellants' invention, it was not possible to make fludarabine phosphate at such purities due to the destruction of some of the fludarabine phosphate during crystallization.

(6) ISSUES

1. Whether claims 5-16, on appeal, are unpatentable under 35 USC §103 for being obvious to one of ordinary skill in the art over U.S. Patent No. 4,357,324 (Montgomery).

a. Are Appellants required to demonstrate that the claimed purified fludarabine phosphate has a separate utility or unique property when one of skill in the art cannot produce such a purified product?

(7) GROUPING OF THE CLAIMS

The claims stand or fall together.

(8) APPELLANT'S ARGUMENTS

I. Summary of Telephone Conference

Below is a summary of the only substantive telephone conference with the examiner.

On August 25, the Examiner indicated that the accompanying declaration was insufficient because it did not demonstrate a separate utility or a unique property per *Ex parte Reed, et al.*, 135 USPQ 34 (CCPA 1961). Appellants countered that *Ex Parte Reed, et al.*, was not applicable, and cited *In re Hoeksema*, 158 USPQ 596 (CCPA 1968) as the applicable case law. Appellants asserted that following the holding in *In re Hoeksema*, the claims should be indicated as allowed.

II. Claim Rejections Under 35 USC §103

Claims 5-16 stand rejected as allegedly being unpatentable over US Patent No. 4,357,324 (Montgomery). Appellants respectfully traverse these rejections.

A. Evidence in the record establishes that one of skill in the art could not make a fludarabine phosphate at the claimed purity prior to Appellants' invention.

Appellants submitted a finalized declaration on August 28, 2003, now entered, it is believed. The declaration provides evidence that one of skill in the art using conventional purification techniques could not obtain a purity of 99.5% or greater. Therefore, the declaration establishes that the claimed purity was not obtainable by one

of skill in the art. The declaration speaks for itself.

B. The purity obtained by the present invention is not merely experimental error.

The action alleged that there is only a .03% difference between that of Montgomery's fludarabine phosphate and the claimed purity. The action concluded that taking into account experimental error, the difference is insignificant and that the claimed composition remains obvious.

Appellants again refer to the declaration establishing that the purities reported were determined to four significant figures, with the only uncertain digit being in the hundredths position. This precision clearly demonstrates that an error in the hundredths position of the largest degree would not cause the best possible prior art 99.14% purity value to overlap with a purity of 99.5% as claimed. This difference is not merely experimental error.

C. *Ex Parte Reed et al.* is not applicable.

Ex Parte Reed et al. is not applicable in the present case. Particularly, *Ex Parte Reed et al.* pertained to compounds of the group consisting of α-lymphatic acid, β-lymphatic acid, and the esters and salts thereof, as well as the water-soluble non-toxic salts of α-lipoic acid. Prior to the Appellants' invention, it was established that the acid was present in the liver and could be isolated, although the method of isolation was difficult. However, it was not impossible. Consequently, this case is not applicable to the present application because before Appellants' invention, it was not possible to obtain a purity of at least 99.5% of fludarabine phosphate. In marked contrast, the facts in *Ex Parte Reed, et al.*, established that it was possible to obtain the isolated compound, although such a process was difficult. Consequently, Appellants respectfully submit that *Ex Parte Reed et al.* is not applicable to the present case.

D. The facts before the Board in the present case are similar to those *In re Hoeksema.*

In re Hoeksema **pertained to a compound claim of an N-psicofuranoside. This claimed compound was rejected over a compound disclosed in a patent to De Boer. The De Boer compound was the same as the claimed compound except the prior art compound contained a primary amino group, which was not present in the claimed compound. Appellant submitted an affidavit stating that the claimed compound was unavailable to the public for preparing the claimed alkylamino and di-alkylamino compounds.**

The court held that the Patent Office citation of the De Boer patent rendered Appellant's claimed compounds *prima facie* obvious. Thus, the burden was shifted to the Appellant to demonstrate that its claimed compounds were patentable. The court held that the affidavit demonstrating that prior to Appellants' invention, it was not possible to produce Appellants' compound, established the patentability of the claimed compounds. Particularly, the absence of a known or obvious process for making the claimed compounds overcomes the presumption that the compounds are obvious, based on the close relationships between their structures and those of the prior art compounds.

In the present case, the Office has alleged that the presently claimed purity of fludarabine phosphate is unpatentable because one of skill in the art would conduct multiple purifications to produce the purified product. However, Appellants have submitted in the record, a declaration by one of skill in the art attesting that conventional purification methods are unsatisfactory for producing the claimed purity, including multiple repetitions of a given purification technique. See, e.g., first full paragraph on page 2 of the declaration, and the paragraph bridging pages 1-2 of the specification. Consequently, Appellants respectfully submit that they have established that the cited prior art is non-enabling. Following the holding in *In re Hoeksema*, Appellants respectfully submit the claim rejections should be reversed.

(9) CONCLUSION

For all of the above reasons, it is urged that the decision of the Examiner rejecting claims 5-16 on appeal, is in error and should be reversed.

Respectfully submitted,

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(10) APPENDIX OF CLAIMS

Claims 1-4 cancelled.

4. **Fludarabine-phosphate with a purity of at least 99.5%.**

5. **Fludarabine-phosphate with a purity of greater than 99.55%.**

6. **Fludarabine-phosphate with a purity of greater than 99.6%.**

7. **Fludarabine-phosphate with a purity of greater than 99.7%.**

8. **Fludarabine-phosphate with a purity of greater than 99.8%.**

9. **Fludarabine-phosphate with a purity of greater than 99.85%.**

10. **Fludarabine phosphate of claim 5 obtained in a quantity greater than one kilogram.**

11. **Fludurabine phosphate of claim 6 obtained in a quantity greater than one kilogram.**

12. **Fludurabine phosphate of claim 7 obtained in a quantity greater than one kilogram.**

13. **Fludurabine phosphate of claim 8 obtained in a quantity greater than one kilogram.**

14. **Fludurabine phosphate of claim 9 obtained in a quantity greater than one kilogram.**

15. **Fludurabine phosphate of claim 10 obtained in a quantity greater than one kilogram.**

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